

IN THE CLAIMS:

1-7. (Cancelled)

8. (Currently amended) An isolated nucleic acid molecule encoding a mutant or variant ~~ion channel subunit sodium channel, voltage gated, type 1, alpha subunit (SCN1A) polypeptide, wherein the isolated nucleic acid molecule comprises a nucleotide sequence comprising~~ a mutation event selected from the group consisting of c.1152G→A (SEQ ID NO: 2), c.1183G→C (SEQ ID NO: 3), c.1207T→C (SEQ ID NO: 4), c.1237T→A (SEQ ID NO: 5), c.1265T→A (SEQ ID NO: 6), and c.5339T→C (SEQ ID NO: 8) ~~as compared to SEQ ID NO: 96, the mutation events set forth in the following Table:~~

Subunit Gene	Exon/Intron	DNA Mutation	<u>SEQ ID NO:</u>
SCN1A	Exon 5	c664C→T	1
SCN1A	Exon 8	c1152G→A	2
SCN1A	Exon 9	c1183G→C	3
SCN1A	Exon 9	c1207T→C	4
SCN1A	Exon 9	c1237T→A	5
SCN1A	Exon 9	c1265T→A	6
SCN1A	Exon 21	c4219C→T	7
SCN1A	Exon 26	c5339T→C	8
SCN1A	Exon 26	c5674C→T	9
SCN1B	Exon 3	c254G→A	
SCN2A	Exon 6A	c668G→A	
SCN2A	Exon 16	c2674G→A	
SCN2A	Exon 17	c3007C→A	
SCN2A	Exon 19	c3598A→G	
SCN2A	Exon 20	c3956G→A	
SCN2A	Exon 12	c1785T→C	
SCN2A	Exon 27	c4919T→A	
SCN1A	Intron 9	IVS9-1G→A	
SCN1A	Intron 23	IVS23+33G→A	
SCN2A	Intron 7	IVS7+61T→A	
SCN2A	Intron 19	IVS19-55A→G	
SCN2A	Intron 22	IVS22-31A→G	
SCN2A	Intron 2	IVS2-28G→A	
SCN2A	Intron 8	IVS8-3T→C	
SCN2A	Intron 11	IVS11+49A→G	
SCN2A	Intron 11	IVS11-16C→T	
SCN2A	Intron 17	IVS17-71C→T	

SCN2A	Intron 17	IVS17-74delG
SCN2A	Intron 17	IVS17-74insG
CHRNA5	Exon 4	c400G→A
CHRNA2	Exon 4	c373G→A
CHRNA3	Exon 2	c110G→A
CHRNA2	Exon 4	c351C→T
CHRNA2	Exon 5	c771C→T
CHRNA3	Exon 2	c159A→G
CHRNA3	Exon 4	c291G→A
CHRNA3	Exon 4	c345G→A
CHRNA2	Intron 3	IVS3-16C→T
CHRNA3	Intron 3	IVS3-5T→C
CHRNA3	Intron 4	IVS4+8G→C
KCNQ2	Exon 1	c204-c205insC
KCNQ2	Exon 1	c1A→G
KCNQ2	Exon 1	c2T→C
KCNQ2	Exon 8	c1057C→G
KCNQ2	Exon 11	c1288C→T
KCNQ2	Exon 14	c1710A→T
KCNQ2	Exon 15	c1856T→G
KCNQ2	Intron 9	IVS9+(46-48)delCCT
KCNQ3	Intron 11	IVS11+43G→A
KCNQ3	Intron 12	IVS12+29G→A
GABRB1	Exon 5	c508C→T
GABRB1	Exon 9	c1329G→A
GABRB1	Exon 8	c975C→T
GABRG3	Exon 8	c995T→C
GABRA1	5' UTR	c-142A→G
GABRA1	5' UTR	c-31C→T
GABRA2	3' UTR	c1615G→A
GABRA5	5' UTR	c-271G→C
GABRA5	5' UTR	c-228A→G
GABRA5	5' UTR	c-149G→C
GABRB2	5' UTR	c-159C→T
GABRB2	3' UTR	c1749C→T
GABRPi	5' UTR	c-101C→T
GABRB1	Intron 1	IVS1+24T→G
GABRB1	Intron 6	IVS6+72T→G
GABRB1	Intron 7	IVS7-34A→G
GABRB3	Intron 1	IVS1-14C→T
GABRB3	Intron 7	IVS7+58delAA
GABRD	Intron 6	IVS6+132insC
GABRD	Intron 6	IVS6+130insC
GABRD	Intron 6	IVS6+73delCGCGCCCCACCG CCCCCTTCCGGCG

GABRG3

Intron 8

IVS8-102C →T

has occurred.

9. (Currently amended) An The isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in of claim 8, wherein a cDNA derived therefrom comprises the sequence set forth in any one of SEQ ID NOS: 1-72 SEQ ID NOS: 2-6 and 8.
10. (Currently amended) An The isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in of claim 8, wherein a cDNA derived therefrom has consists of the sequence set forth in any one of SEQ ID NOS: 1-72 SEQ ID NOS.: 2-6 and 8.
11. (Currently Amended) AnThe isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in of claim 8, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype.
12. (Currently Amended) An The isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in of claim 8, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce one or more disordersa disorder associated with ion channel dysfunction, including but not restricted to, hyper- or selected from the group consisting of hyper-kalemic periodic paralysis, hypo-kalemic periodic paralysis, myotonia[[s]], malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease,

hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness, and total colour-blindness.

13. (Currently Amended) An The isolated nucleic acid molecule ~~encoding a mutant or variant ion channel subunit as claimed in~~ of claim 8, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype when expressed in combination with one or more additional mutations or variations in said an ion channel subunit gene[[s]].
14. (Currently Amended) An The isolated nucleic acid molecule ~~encoding a mutant or variant ion channel subunit as claimed in~~ of claim 8, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce ~~one or more disorders~~ a disorder associated with ion channel dysfunction, ~~including but not restricted to, hyper-~~ or selected from the group consisting of hyper-kalemic periodic paralysis, hypo-kalemic periodic paralysis, myotonia[[s]], malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness, and total colour-blindness, when expressed in combination with one or more additional mutations or variations in said an ion channel subunit gene[[s]].
15. (Currently amended) An isolated nucleic acid molecule comprising ~~any one of the nucleotide sequences~~ as set forth in SEQ ID NOS: 1-72 any of SEQ ID NOS.: 2-6 and 8.
16. (Currently amended) An isolated nucleic acid molecule consisting of ~~any one of the nucleotide sequences~~ as set forth in SEQ ID NOS: 1-72 any of SEQ ID NOS.: 2-6 and 8.
- 17-29. (Canceled)

30. (Currently Amended) An expression vector comprising [[a]] the isolated nucleic acid molecule as claimed in of claim 8.
31. (Currently amended) A cell comprising at least one expression vector as claimed in of claim 30.
32. (Currently amended) A cell as claimed in The cell of claim 31, wherein the cell comprises comprising two or more expression vectors of claim 30.
33. (Currently amended) An isolated cell comprising at least one ion channel type, wherein the or each ion channel type incorporates at least one mutant sodium channel, voltage gated, type 1, alpha subunit (SCN1A) polypeptide, said mutantSCN1A polypeptide being a mutant or variant ion channel subunit wherein comprising a mutation event selected from the group consisting of W384X (SEQ ID NO: 74), A395P (SEQ ID NO: 75), F403L (SEQ ID NO: 76), Y413N (SEQ ID NO: 77), V422E (SEQ ID NO: 78), and M1780T (SEQ ID NO: 80) as compared to SEQ ID NO: 97, the mutation events set forth in the following Table:

Subunit Gene Amino Acid Change

SCN1A	R222X
SCN1A	W384X
SCN1A	A395P
SCN1A	F403L
SCN1A	Y413N
SCN1A	V422E
SCN1A	R1407X
SCN1A	M1780T
SCN1A	R1892X
SCN1B	R85H
SCN2A	R223Q
SCN2A	V892I
SCN2A	L1003I
SCN2A	T1200A
SCN2A	R1319Q
CHRNA5	V134I
CHRNA2	A125T

CHRNA3	R37H
KCNQ2	K69fsX119
KCNQ2	M1V
KCNQ2	M1T
KCNQ2	R353G
KCNQ2	R430X
KCNQ2	R570S
KCNQ2	L619R

34. (Currently amended) A cell as claimed in The isolated cell of claim 33, comprising ion channels that incorporate wherein the isolated cell comprises two or more mutant SCN1A polypeptides.
35. (Currently amended) A cell as claimed in The isolated cell of claim 33 34, comprising two or more ion channel types each incorporating one or more mutant polypeptides wherein the two or more mutant SCN1A polypeptides are present in two or more ion channel types.
36. (Currently amended) A method of preparing a polypeptide, the method comprising the steps of:
- (1) culturing cells as claimed in the cell of claim 31 under conditions effective for expressing the polypeptide production encoded by the expression vector; and
 - (2) harvesting the polypeptide encoded by the expression vector.
37. (Original) A polypeptide prepared by the method of claim 36.
- 38-85. (Cancelled)
86. (Currently amended) An isolated polypeptide encoded by an the isolated nucleic acid molecule as claimed in of claim 8.